UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,512	10/31/2003	George Nelson Bennett	61683-00003USPT	3570

51738 7590 09/18/2006

BAKER & MCKENZIE LLP
Pennzoil Place, South Tower
711 Louisiana, Suite 3400
HOUSTON, TX 77002-2716

EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,512	BENNETT, GEORGE NELSON	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. The objection to claim 5 is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Borokov et al (WO 01/11058).

Borokov teaches a method of claims 1 and 6 for the assembly of large DNA fragments (see abstract), comprising:

a) manipulating a replicon to comprise in order a final excision site, a first fragment, a first excision site and a first recombinase site (see page 31, lines 5-33 and figure 8B, where the pMON38288 plasmid comprises a Lox511 first and final excision site, a first fragment which could be HygB, a first excision site which is the LoxA02 and a first recombinase site which is loxP05);

b) manipulating a first vector to comprise in order the first recombinase site from step a), undesired vector sequences, the first excision site from step a), a second fragment, and a

second excision site (see page 31, lines 5-19 and figure 8B which shows the pMON38271basic vector with a Lox511 site excision site, undesired vector sequences, and the LoxP02 excision site);

c) inserting the first vector into the replicon using a first recombinase so that the two first site specific excision sites are oriented in an appropriate orientation for excision with undesired vector sequences therebetween (see page 31, lines 11-19 and figures 9A, which show insertion of the first vector into the replicon so that the site specific excisionases will excise the undesired sequence);

d) treating the replicon with a first excisionase to remove the undesired vector sequences and bring the second fragment adjacent to the first fragment (see figure 9B, where the HygB gene is placed adjacent to the plac promoter);

e) manipulating a second donor vector to comprise a first recombinase site from step a), undesired vector sequences, the second excision site from step b), a third fragment and the first excision site from step a) (see page 31, lines 20-27 and figure 8C, where pMON38997 has the first recombinase site of loxP05, undesired vector sequences, the second excision site of LoxP02, a third fragment which is the Spc gene, and the first excision site of Lox511)

f) inserting the second vector into the replicon using the first recombinase so that the two second site specific excision sites are oriented in an appropriate orientation for excision with undesired vector sequences therebetween (see page 31, lines 20-27, where Shuttle II inserts the spectinomycin gene)

g) treating the replicon with a second excisionase to remove the undesired vector sequences and bring the third fragment adjacent to the second fragment (see apge 31, lines 20-27, where unwanted vector sequences are removed);

h) repeating steps b-g using at least the first and second excisionases to make an assembled DNA, wherein the final vector also comprises the final excision site 5' to all other sequences and in an appropriate orientation for excision (see page 31, lines 28-33, where the process can be repeated), and

i) excising and circularizing the assembled DNA with a final excisionase (see page 31, lines 5-33, where the final product results from excision and results in a circular molecule (see figure 9A as well)).

With regard to claim 2, Borokov teaches in vivo assembly (see page 25, example 3).

With regard to claim 3, Borokov teaches in vitro assembly (see page 24, example 2).

With regard to claims 4, 7, Borokov generically teaches that any known recombinase system can be used and expressly teaches Cre, Lox and Frt.(see page 15, lines 14-31).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 4, 5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borokov et al (WO 01/11058) in view of Cheo et al (U.S. 2002/0007051).

Borokov teaches a method of claims 1 and 6 for the assembly of large DNA fragments (see abstract), comprising:

a) manipulating a replicon to comprise in order a final excision site, a first fragment, a first excision site and a first recombinase site (see page 31, lines 5-33 and figure 8B, where the pMON38288 plasmid comprises a Lox511 first and final excision site, a first fragment which could be HygB, a first excision site which is the LoxA02 and a first recombinase site which is loxP05);

b) manipulating a first vector to comprise in order the first recombinase site from step a), undesired vector sequences, the first excision site from step a), a second fragment, and a

second excision site (see page 31, lines 5-19 and figure 8B which shows the pMON38271basic vector with a Lox511 site excision site, undesired vector sequences, and the LoxP02 excision site);

c) inserting the first vector into the replicon using a first recombinase so that the two first site specific excision sites are oriented in an appropriate orientation for excision with undesired vector sequences therebetween (see page 31, lines 11-19 and figures 9A, which show insertion of the first vector into the replicon so that the site specific excisionases will excise the undesired sequence);

d) treating the replicon with a first excisionase to remove the undesired vector sequences and bring the second fragment adjacent to the first fragment (see figure 9B, where the HygB gene is placed adjacent to the plac promoter);

e) manipulating a second donor vector to comprise a first recombinase site from step a), undesired vector sequences, the second excision site from step b), a third fragment and the first excision site from step a) (see page 31, lines 20-27 and figure 8C, where pMON38997 has the first recombinase site of loxP05, undesired vector sequences, the second excision site of LoxP02, a third fragment which is the Spc gene, and the first excision site of Lox511)

f) inserting the second vector into the replicon using the first recombinase so that the two second site specific excision sites are oriented in an appropriate orientation for excision with undesired vector sequences therebetween (see page 31, lines 20-27, where Shuttle II inserts the spectinomycin gene)

g) treating the replicon with a second excisionase to remove the undesired vector sequences and bring the third fragment adjacent to the second fragment (see apge 31, lines 20-27, where unwanted vector sequences are removed);

h) repeating steps b-g using at least the first and second excisionases to make an assembled DNA, wherein the final vector also comprises the final excision site 5' to all other sequences and in an appropriate orientation for excision (see page 31, lines 28-33, where the process can be repeated), and

i) excising and circularizing the assembled DNA with a final excisionase (see page 31, lines 5-33, where the final product results from excision and results in a circular molecule (see figure 9A as well)).

With regard to claim 2, Borokov teaches in vivo assembly (see page 25, example 3).

With regard to claim 3, Borokov teaches in vitro assembly (see page 24, example 2).

With regard to claims 4, 7, Borokov generically teaches that any known recombinase system can be used and expressly teaches Cre, Lox and Frt.(see page 15, lines 14-31).

Borokov does not teach the Tn3 or Hin recombination systems. Borokov does teach assembly of more than 10 kb (see page 16, line 6), but does not discuss larger fragments.

Cheo teaches the equivalence of a variety of recombination systems including Cre-lox, Tn3 and Hin for recombination (see paragraph 055, page 6). Cheo further teaches that nucleic acid fragments formed by recombination can be between 0.5 and 300 kb (see page 0408, page 46).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize any known equivalent recombination system

since Borokov expressly teaches that multiple classes of recombination sites can bee used (see page 15, lines 14-31) and since Cheo teaches the equivalence of the different recombination systems. MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Further, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that nucleic acids could be between 0.5 to 300 kb since Cheo expressly teaches that, dependent upon the number of function segments desired, the size may range up to 300 kb (see paragraph 0408, page 46).

Response to Declaration under 1.131

6. The Declaration filed on August 25, 2006 under 37 CFR 1.131 has been considered but is ineffective to overcome the Cheo et al reference.

7. The declaration indicates that the invention was conceived prior to October 31, 2001. While this date is prior to the publication date of Cheo et al (U.S. 2002/0007051) and prevents Cheo from functioning as a 102(a) type reference in the 103 rejection, Cheo was filed December 11, 2000 and is based upon a provisional filed December 10, 1999. There is no question that Cheo is a 102(e) type reference as of December 11, 2000 and may so be used in a 103 rejection. Therefore, the date necessary to antedate

the Cheo reference is at least December 11, 2000, and based upon a review of the provisional, which appears to provide support of the same subject matter, probably December 10, 1999. Therefore, the Cheo references remains applicable.

Response to Arguments

8. Applicant's arguments filed August 25, 2006 have been fully considered but they are not persuasive.

Applicant argues that Borokov is not anticipatory because of a difference between the terms "excisionase" and "recombinase". These terms are not defined in the specification. The specification does make it abundantly clear that some "recombinases" can function as "excisionases" (see page 3, paragraph 13 of the specification) solely when the recombinases are permitted to excise. Borokov teaches the use of recombinases which function to excise sequences, meeting the only element required by the definition in the specification.

Applicant's entire argument relating to the status of LoxP02, LoxP05 and Lox511 are definitional. The specification supports defining these recombinases as "excisionases" when they function to excise sequences. Applicant points to no evidence or support for a contrary interpretation.

Applicant then argues that the function of Borokov would result in DNA fragments punctuated by "dead " recombinase sites. The claims do not distinguish from this method. Applicant points to no claim limitation which structurally distinguishes from the Borokov reference.

Finally, as noted above, the declaration is insufficient to overcome the Cheo reference, since the date stated by the Declarant is not prior to the filing date of the Cheo reference.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
9/13/06